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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/715,983	11/20/2000	Brett P. Monia	ISPH-0519	6803

7590 05/07/2003

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EXAMINER
ZARA, JANE J

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/715,983	Monia et al
Examiner	**Art Unit**
Jane Zara	1635

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Feb 20, 2003* .

2a) X This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *24-31 and 40-47* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) X Claim(s) *24-31 and 40-47* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1	Notice of References Cited (PTO-892)	4	Interview Summary (PTO-413) Paper No s.
2	Notice of Draftsperson's Patent Drawing Review (PTO-948)	5	Notice of Informal Patent Application (PTO-152)
3	Information Disclosure Statement s (PTO-1449) Paper No s.	6	Other:

DETAILED ACTION

This Office action is in response to the communication filed February 20, 2003, Paper No. 10.

Claims 24-31, 40-47 are pending in the instant application.

Any rejections not repeated in this Office action are hereby withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Maintained Rejections

Claims 24-31 and 40-47 are rejected under 35 U.S.C. 112, first paragraph, for lacking enablement over the scope claimed for the reasons of record set forth in the Office action mailed November 19, 2002, Paper No. 9.

Applicant's arguments filed February 20, 2003 have been fully considered but they are not persuasive. Applicants argue that the full scope of the claims is enabled, which scope comprises decreasing blood glucose and insulin levels in any organism comprising the administration of antisense oligonucleotides between 8-30 nucleobases in length, which antisense specifically target and inhibit the expression of human PI3K p85 of SEQ ID NO: 1. Contrary to Applicants assertions, however, the instant disclosure teaches the ability to decrease blood glucose and insulin levels using mouse models, which models are reasonable for analogous treatment

applications in humans. The ability to achieve these treatment effects in mice, as well as knowing the homology between mouse and human PI3K p85, however, is not necessarily predictive of the ability to achieve these treatment effects in any and/or all organisms comprising the administration of antisense oligonucleotides that specifically target and inhibit the expression of human PI3K p85 of SEQ ID NO: 1.

Applicants additionally argue that the full scope of the claims are enabled, including the ability to prevent or delay onset of increased blood glucose or insulin levels in any organism comprising the administration of antisense oligonucleotides between 8 and 30 nucleobases that specifically target and inhibit the expression of PI3K p85 of SEQ ID NO: 1, because well designed pharmacological studies in vivo in animals are predictive of the production of the same effects in humans, including rodent models for blood glucose and insulin responses in humans.

The correlation or appropriateness of the animal models provided in the instant application for predicting efficacy in humans for purposes of enablement is not the issue or issues addressed in the instant scope of enablement rejection. Contrary to Applicants' assertions, no evidence has been provided in the instant disclosure or in the known scientific literature, for the ability to delay the onset or prevent increased blood glucose or insulin levels in an organism comprising the administration of antisense that target and specifically inhibit the expression of PI3K p85. The instant disclosure provides evidence for the ability to decrease blood glucose levels or insulin levels in mice comprising administration of antisense between 8-30 nucleobases that specifically target and inhibit the expression of human PI3K p85. The ability to decrease blood glucose levels

or insulin levels in an organism (i.e mouse or humans) comprising the administration of these antisense, however, is not predictive of the ability to delay the onset or prevent increasing blood glucose or insulin levels. The treatment effects demonstrated are not extrapolatable to prevention. It would require undue experimentation beyond that which has been provided in the instant disclosure, or which exists in the art, to prevent or delay the onset of increasing blood glucose or insulin levels in any organism comprising the administration of antisense. Therefore, the claimed invention is not enabled for this broad scope.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RAM SHUKLA
PRIMARY EXAMINER

JZ

May 4, 2003